UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,887	03/29/2002	Bruce M. Boman	1657/1022	2568

29932 7590 10/21/2005

PALMER & DODGE, LLP
PAULA CAMPBELL EVANS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,887	BOMAN ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-45* is/are pending in the application.

4a) Of the above claim(s) *1-26,29,31-33,35-42 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,28,30,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number PCT/US00/21606.

Claim 34 has been canceled.

Claims 1-33 and 35-45 are currently pending.

Election/Restrictions

1. Applicant's election of Group 114, claims 27-28, 30, 34 and 43-44 as they read upon SEQ ID NO: 46, in the reply filed on November 10, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). It is noted that SEQ ID NO: 47, as presently recited in the claims, is the amino acid sequence deduced to be encoded by SEQ ID NO: 46.

Claims **1-26, 29, 31-33, 35-42 and 45 stand withdrawn** from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 10, 2004.

Claims 27-28, 30 and 43-44 are the subject of examination in the present Office Action.

In view of Applicant's amendment filed July 14, 2005 only the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 27-28, 30, 43 and 44 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was previously stated: "The claims are most broadly drawn to the detection of a putative polypeptide that may be encoded by SEQ ID NO: 46, determining the phenotype of a cell based upon differential expression of the putative polypeptide encoded by SEQ ID NO: 46, or detecting a tumor based upon expression of the putative polypeptide encoded by SEQ ID NO: 46.

The putative peptide has been reverse transcribed from the cDNA sequence of SEQ ID NO: 46. SEQ ID NO: 46 was isolated from a library obtained from HCT116 cells, a cultured human colon cancer cell line (pages 96 and 100-101 of the specification, for example). The cDNA was identified in the specification as CATX-15 (SEQ ID NO: 46), is 3032 nucleotides in length and "appears to be a complete cDNA" (page 100, line 24 for example). The isolated cDNA was subjected to analysis to predict open reading frames within the sequence and an open reading frame encoding for a putative 246 amino acid polypeptide (SEQ ID NO: 47) was identified (paragraph bridging pages 100-101 for example). A 246 amino acid polypeptide requires only a 741 nucleotide long (including a stop codon) mRNA encoding it. There is no indication in the specification, however, that the actual polypeptide of SEQ ID NO: 47 has ever been expressed from the cDNA or isolated from a natural tissue source, nor is there any disclosure of any other polypeptide sequence being identified from the cDNA of SEQ ID NO: 46. Accordingly, Applicant has not demonstrated that any polypeptide encoded by SEQ ID NO: 46, other than the putative SEQ ID NO: 47 was in Applicant's possession at the time the application was filed.

Furthermore, the claims are drawn to methods of detecting a polypeptide encoded by SEQ ID NO: 46 in order to phenotype a cell or to differentiate a cell from a "normal" cell. The instant specification demonstrated the presence of SEQ ID NO: 46 in a single clonal line of human cancer cells and its absence in normal colonic epithelial cells isolated from a single subject (table 2 for example). However, no polypeptide encoded by SEQ ID NO: 46, including the putative SEQ ID NO: 47, has been demonstrated to be present or absent in any type of cell. There is no indication that a polypeptide encoded by SEQ ID NO: 46, or a subsequence thereof, was expressed in the colonic cancer cells, not expressed in the normal colonic epithelial cells, or differentially expressed between any cell types. Further, because there is no evidence that a polypeptide encoded by SEQ ID NO: 46 even exists, there is no evidence that antibodies to such a polypeptide have been generated. The recitation of antibodies for detecting the polypeptide in cells in the instant claims is based solely upon the identification of a putative open reading frame within the sequence of SEQ ID NO: 46, not upon the isolation of any actual polypeptide product.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

The sole support for the claimed method is in Table 2 and at the paragraph bridging pages 100-101 of the instant specification showing that a nucleic acid molecule reversed transcribed to yield SEQ ID NO: 46 was present in a single clonal human colon cancer cell line but was not present in cells isolated from a single normal colonic epithelium tissue. This is insufficient to support the recitation in the claims of methods of determining the presence or absence of a polypeptide encoded by SEQ ID NO: 46 using antibodies to the polypeptide, determining the phenotype of a cell based upon expression of a polypeptide encoded by SEQ ID NO: 46 or detecting differential expression of a polypeptide encoded by SEQ ID NO: 46 in a cell as provided by the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001."

Applicant's arguments filed July 14, 2005 have been fully considered but they are not persuasive.

Applicant has amended the claims to specifically recite the amino acid sequence of SEQ ID NO: 47, which is putatively encoded by the nucleic acid molecule of SEQ ID NO: 46. However, as stated previously, the fact remains that there is no evidence that the amino acid sequence of SEQ ID NO: 47 was ever produced in the colon cancer cells from which the amino acid sequence of SEQ ID NO: 46 was identified. SEQ ID NO: 47 remains a putative polypeptide sequence and there is no showing that expression of a polypeptide with the sequence defined by SEQ ID NO: 47 in a cell would be indicative of cancer. SEQ ID NO: 46 was not isolated as a singular entity from the colon cancer cells of the sample, but was identified as a probable open reading frame within a nucleic acid sequence more that 4 times the size of SEQ ID NO: 46. There is also a lack of evidence that, even if the polypeptide of SEQ ID NO: 47 is ever produced by any cell, that expression of SEQ ID NO: 47 would be differential between normal cells and cancer cells. Therefore, the specification has not adequately shown possession of a method wherein the expression of SEQ ID NO: 47 would be determinative for any cancerous or precancerous phenotype. In Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), the Court noted "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

3. Claims 27-28, 30, 43 and 44 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It was previously stated: "The claims are most broadly drawn to the detection of a putative polypeptide that may be encoded by SEQ ID NO: 46, determining the phenotype of a cell based upon differential expression of the putative polypeptide encoded by SEQ ID NO: 46, or detecting a tumor based upon expression of the putative polypeptide encoded by SEQ ID NO: 46.

The putative peptide has been reverse transcribed from the cDNA sequence of SEQ ID NO: 46. SEQ ID NO: 46 was isolated from a library obtained from HCT116 cells, a cultured human colon cancer cell line (pages 96 and 100-101 of the specification, for example). The cDNA was identified in the specification as CATX-15 (SEQ ID NO: 46), is 3032 nucleotides in length and "appears to be a complete cDNA" (page 100, line 24 for example). The isolated cDNA was subjected to analysis to predict open reading frames within the sequence and an open reading frame encoding for a putative 246 amino acid polypeptide (SEQ ID NO: 47) was identified (paragraph bridging pages 100-101 for example). A 246 amino acid polypeptide requires only a 741 nucleotide long (including a stop codon) mRNA encoding it. There is no indication in the specification, however, that the actual polypeptide of SEQ ID NO: 47 has ever been expressed from the cDNA or isolated from a natural tissue source, nor is there any disclosure of any other polypeptide sequence being identified from the cDNA of SEQ ID NO: 46. Accordingly, Applicant has not demonstrated that any polypeptide encoded by SEQ ID NO: 46, other than the putative SEQ ID NO: 47 was in Applicant's possession at the time the application was filed.

Furthermore, the claims are drawn to methods of detecting a polypeptide encoded by SEQ ID NO: 46 in order to phenotype a cell or to differentiate a cell from a "normal" cell. The instant specification demonstrated the presence of SEQ ID NO: 46 in a single clonal line of human cancer cells and its absence in normal colonic epithelial cells isolated from a single subject (table 2 for example). However, no polypeptide encoded by SEQ ID NO: 46, including the putative SEQ ID NO: 47, has been demonstrated to be present or absent in any type of cell. There is no indication that a polypeptide encoded by SEQ ID NO: 46, or a subsequence thereof, was expressed in the colonic cancer cells, not expressed in the normal colonic epithelial cells, or differentially expressed between any cell types. Further, because there is no evidence that a polypeptide encoded by SEQ ID NO: 46 even exists, there is no evidence that antibodies to such a polypeptide have been generated. The recitation of antibodies for detecting the polypeptide in cells in the instant claims is based solely upon the identification of a putative open reading frame within the sequence of SEQ ID NO: 46, not upon the isolation of any actual polypeptide product.

Applicant has amended the claims to specifically recite the amino acid sequence of SEQ ID NO: 47, which is putatively encoded by the nucleic acid molecule of SEQ ID NO: 46.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Despite Applicant's amendment to positively recite the amino acid sequence rather than a polypeptide encoded by SEQ ID NO: 46, there is still no evidence that the amino acid sequence of SEQ ID NO: 47 was ever produced in the colon cancer cells from which the amino acid sequence of SEQ ID NO: 46 was identified. SEQ ID NO: 47 remains a putative polypeptide sequence and there is no showing that expression the polypeptide of SEQ ID NO: 47 in a cell would be indicative of cancer. SEQ ID NO: 46 was not isolated as a singular entity from the colon cancer cells of the sample, but was identified as a probable open reading frame within a nucleic acid sequence more that 4 times the size of SEQ ID NO: 46. There is also a lack of evidence that, even if the polypeptide of SEQ ID NO: 47 is ever produced by any cell, that expression of SEQ ID NO: 47 would be differential between normal cells and cancer cells. Therefore, the specification has not adequately shown that the artisan would be able to predict that expression of SEQ ID NO: 47 would be determinative for any cancerous or precancerous phenotype.

The following NEW GROUND of rejection has been necessitated by Applicant's amendment filed July 14, 2005.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites the limitation "the cell" in line 3 of the claim after amendment. There is no antecedent basis for this limitation in the claim. Claim 30 has been amended to be an independent claim. There is no previous recitation of a "cell" in the claim.

Conclusion

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
October 14, 2005

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644